REMARKS

I. PRELIMINARY REMARKS

Claim 55-65 are pending and currently under examination and are directed to a method for generating a composition of contiguous overlapping peptide fragments. The present invention relates generally to immunotherapy methods providing reduced risk of anaphylaxis. In particular, the invention is directed to the preparation of improved compositions of contiguous overlapping peptide fragments (COPs) for selected allergens wherein the fragments are capable of inducing a T cell response in patients who are hypersensitive to the allergen but wherein administration of the compositions of the invention results in lower levels of IgE stimulation activity.

Claim 55 has been amended to specify that IgE binding activity is detected by both *in vitro* and *in vivo* tests. In addition, claim 63 was amended to incorporate the limitations of claim 64 which was canceled. Finally, claim 65 has been amended to more clearly recite the nature of the intradermal test. This amendment is supported at page 4, lines 22-24 of the disclosure and does not introduce new matter.

II. OUTSTANDING REJECTIONS

Claims 55-61 have been rejected under 35 U.S.C. 102(b) as being anticipated by Spertini WO 01/88085.

Claims 55 and 61-62 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Spertini WO 01/88085 in view of Shanti et al., The Journal of Immunology, Vol. 151, 5354-5363, No. 10, 11/15/1993.

Claims 55 and 63-65 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Spertini WO 01/88085 in view of Spertini et al., C23 Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in J. Allergy Clin. Immunol., 105(1- pt. 2):S278.

III. PATENTABILITY ARGUMENTS

A. The Rejections of Claims 55-61 Under 35 USC §102 Over Spertini WO 01/88085 Should Be Withdrawn.

The anticipation rejection of claims 55-61 over Spertini WO 01/88085 should be withdrawn because it neither discloses nor teaches selecting peptides with reduced IgE binding activity by use of the combination of an *in vitro* test with an *in vivo* test as required by the foregoing amendment. Although separate elements within the claimed method can be found within Spertini WO 01/88085 there is no teaching of how to select for proper peptides to be used to treat allergic subjects. Moreover, one following the teachings of Spertini WO 01/88085 would not have selected proper peptides because its use of *in vitro* IgE binding tests such as ELISA, immunoblots and dot blots, produces false negative results that use of a skin test would have avoided.

Independent claim 55 has been amended to recite that the detection of IgE binding activity is by *in vitro* testing and by an *in vivo* test and as such the claim is novel over Spertini WO 01/88085 which does not disclose *in vitro* or skin testing. Instead, Spertini WO 01/88085 at page 6, lines 27-30 discloses the use of peptides to tolerize patients by subcutaneous injection and not to check for lower IgE levels. The reference at page 19, lines 13-29 of Spertini WO 01/88085 is to the ability of the peptides to stimulate IgE formation during treatment and not to check for lower IgE binding of the peptides *in vitro*.

Even if Spertini WO 01/88085 were to teach *in vitro* testing for IgE binding to peptide candidates, such a disclosure would be misleading because *in vitro* testing is prone to false negatives. Thus, when Fellrath et al., J. Clin Immunol. Vol 111, No. 4, pp. 854-861 (2003) (a copy of which is attached as Exhibit A) practiced the methods of Spertini WO 01/88085 in the production of PLA 2 bee venom peptides the results of a dot blot testing were positive for IgE binding activity. See p 858, last paragraph to p 859 first paragraph and Fig. 5 of Fellrath which depicts residual IgE binding activity for peptides LSP 1-60 and LSP 90-134 which peptides would have been discarded by practice of the claimed method. Thus, Spertini WO 01/88085 not only fails to disclose the present invention but it teaches away from it.

B. The Rejections of Claims 55, and 61-62 Under 35 USC §103(a) in view of Spertini WO 01/88085 in view of Shanti et al. Should Be Withdrawn.

The rejection of claims 55 and 61-62 under 35 U.S.C. 103(a) as being unpatentable over Spertini WO 01/88085 in view of Shanti et al. (The Journal of Immunology, Vol. 151, 5354-5363, No. 10, 11/15/1993) should be withdrawn because Shanti fails to make up for the deficiencies of Spertini WO 01/88085 with respect to independent claim 55 as described above. Moreover, Shanti teaches away from the present invention by teaching that one of ordinary skill would have performed dot blots for showing the presence of IgE able to bind to COPs. Unexpectedly, COPs do not bind under comparable experimental conditions to serum IgEs of allergic patients. Thus, the method of the claimed invention provides the selection of peptides which, contrary to Shanti's peptides, do not bind IgE on dot blots!

To further elaborate, a positive result with dot blots indicates IgE binding. A negative result, however, may depend upon the technical setup and taken alone is not proof of lowered IgE binding. It could be a false negative! The claimed method which combines *in vitro* assays such as ELISA or dot blots with skin tests ensures the selection of peptides with low IgE binding activity that can be used at high dosages to safely treat patients. Accordingly, the rejection of claims 55 and 61-62 should be withdrawn.

C. The Rejections of Claims 55 and 63-65 Under 35 USC §103(a) in view of Spertini et al. WO 01/88085 in View of Spertini C23 Should Be Withdrawn.

The rejection of claims 55 and 63-65 under 35 U.S.C. 103(a) as being unpatentable over Spertini WO 01/88085 in view of Spertini et al. C23 Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in J. Allergy Clin. Immunol., 105(1- pt. 2):S278 should be withdrawn because Spertini C23 neither makes up for the deficiencies of Spertini WO 01/88085 with respect to the elements of independent claim 55 nor does it teach the elements of dependent claims 63-65 directed to the specifics of the dermal test.

Spertini C23 fails to teach how its COPs were selected and it fails to describe what constitutes "positiveness" in intradermal tests or teach testing for a 5 mm wheal and flare reaction as recited in Applicants' claims. While intradermal tests were known as routine tests to verify skin reactivity during treatment Spertini C23 fails to teach the use of such tests as a

method for selecting proper COPs. Moreover, skin tests alone will not provide the peptides of the present invention.

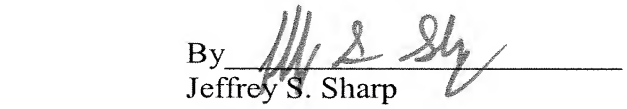
As was discussed above with respect to Fellrath (which is the publication which followed the abstract of Spertini C23) the peptides identified in Spertini C23 would not have been selected using the method of the claimed invention because they show reactivity on dot blots (detectable IgE binding on dot blots and accordingly 3 subjects showing reactivity after treatment with the peptides.) As a further example, peptide LSP 90-134 of Fellrath contains a disulfide bridge as seen by computer structure prediction. It binds IgE *in vitro* as seen by dot blots in Fig. 5 of Fellrath and would not be optimal for treatment and would not have been selected by practice of the claimed invention.

CONCLUSION

For the foregoing reasons, it is submitted that each of claims 55-65 should now be allowed. Should the Examiner wish to discuss any issues of form or substance, she is invited to contact the undersigned attorney at the number below.

Dated: September 26, 2008

Respectfully submitted,

By 

Jeffrey S. Sharp
Registration No.: 31,879
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant